



Selecting an Initial Antiretroviral Therapy (ART) Regimen

An HIV Diagnosis is a Call to Action

In support of the NYSDOH AIDS Institute's January 2018 call to action for patients newly diagnosed with HIV, the guideline committee stresses the following:

- Immediate linkage to care is essential for any person diagnosed with HIV.
- ART dramatically reduces HIV-related morbidity and mortality.
- Viral suppression helps to prevent HIV transmission to sex partners of people with HIV and prevents perinatal transmission of HIV.
- The urgency of ART initiation is even greater if the newly diagnosed patient is pregnant, has acute HIV infection, is ≥ 50 years of age, or has advanced disease. For these patients, every effort should be made to initiate ART immediately, and ideally, on the same day as diagnosis.
- All clinical care settings should be prepared, either on-site or with a confirmed referral, to support patients in initiating ART as rapidly as possible after diagnosis.

Goal of ART

Complete and durable suppression of plasma viremia while minimizing toxicity and maximizing quality of life.

KEY POINTS:

- Properly selected ART may never require a change or adjustment once started.
- Treatment interruptions should be avoided.

Choosing an Initial Regimen

✓ RECOMMENDATIONS

- Clinicians should involve their patients when deciding which ART regimen is most likely to result in patient adherence (AIII).
- Clinicians should perform the following when initiating ART:
 - Assessment for comorbidities that may affect the choice of regimen for initial therapy (AIII).
 - Genotypic resistance testing for the protease and reverse transcriptase genes at diagnosis or at the initial visit if not done previously (All).
 - Baseline testing is not recommended for either integrase resistance or tropism (AIII).
- For patients who have delayed initiation of ART *and* have engaged in high-risk behaviors associated with acquisition of HIV superinfection, genotypic resistance testing should be repeated before choosing the ART regimen (BIII).

Choosing an Initial Regimen

✓ RECOMMENDATIONS, *continued*

- Clinicians should consult with a care provider experienced in ART management when:
 - Baseline resistance requires treatment with a regimen other than the listed preferred or alternative regimens (AIII).
 - Selecting a regimen for patients with extensive comorbidities (BIII), impaired renal function (BIII), HBV or HCV co-infections (BIII), active opportunistic infections (BIII), or very high viral loads (BIII).
- Clinicians should:
 - Ask individuals about their reproductive plans and discuss the use of contraception (AIII).
- Refer to the DHHS guideline when choosing an initial regimen for individuals of childbearing potential.

Choosing an Initial Regimen

✓ RECOMMENDATIONS, *continued*

- A single-tablet regimen or a regimen with once-daily dosing is preferred unless contraindicated by drug-drug interactions, intolerance, allergy, or access (AII).
- For ART-naïve patients, clinicians should (AI):
 - Select an initial ART regimen that is preferred (guideline Table 1).
 - Select an alternative (guideline Table 2) or other (guideline Table 3) regimen only when a preferred initial regimen cannot be used
- Two-drug regimens are not recommended as initial therapy (AII).
- Clinicians or clinical staff should follow up, by telephone or other methods, within 2 weeks after treatment initiation to assess tolerance and adherence. Adherence should be reinforced at regular intervals (AIII).
- Clinicians should obtain a viral load test within 4 weeks after initiation to assess response to therapy (AIII)

Dolutegravir (DTG) Safety Statement

On May 18, 2018, the FDA and the DHHS Antiretroviral Guidelines Panel issued statements in response to preliminary results from a study that reported increased risk of neural tube defects in babies born to mothers who were taking dolutegravir (DTG)-based ART at the time of conception.

Clinicians should refer to the DHHS guideline when choosing an initial regimen for women of childbearing potential: *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*.

General Principles in Choosing an Initial ART Regimen

- Patients should receive 3 active drugs from at least 2 different classes.
- The “backbone” of therapy remains 2 nucleoside reverse transcriptase inhibitors (NRTIs) paired with a non-nucleoside reverse transcriptase inhibitors (NNRTI), or a boosted protease inhibitor (PI), or a boosted or unboosted integrase strand inhibitor (INSTI).
 - INSTI-based regimens are generally the best choice for most patients because of tolerability and durability.
- Two other classes of approved medications, entry inhibitors and fusion inhibitors, are not recommended for initial therapy but may have a role in treatment-experienced patients with extensive drug resistance

3-Drug Regimens Remain the Standard

→ KEY POINT

- Although dual or even monotherapy regimens have been and continue to be studied, they cannot be recommended currently as initial therapy until more data are available. Existing studies show limitations with these regimens in ART-naïve individuals based on pill burden, toxicities, and efficacy, particularly in patients with viral loads $>100,000$ copies/mL or CD4 counts <200 cells/mm³, compared with recommended therapy.

Preferred ART Regimens

- Supported by published clinical evidence.
- Treatment efficacy factors that include:
 - Favorable adherence profiles
 - Lower pill burden
 - Fewer adverse effects
 - Dosing schedules that may be easier for patients to manage

Single- vs Multi-Tablet Regimens

- Advantages of single-tablet regimens (STR): Simplicity, convenience, lower chance of selective non-adherence.
- Disadvantages of STRs:
 - Limited to 3 available regimens
 - Available regimens may contain one or more components not appropriate for the individual patient
 - Do not allow for adjustment of individual components for renal function
 - May be more expensive than the individual components prescribed separately, particularly if available as generic formulations

Factors to Consider & Discuss with Patients

- The patient's age, comorbidities, and pregnancy or conception planning
- ART regimen cost, dosing requirements (daily vs twice-daily), number of pills, pill size, food requirements, known side effects and toxicities
- Drug-drug interactions and food requirements: see full guideline

Comorbid Conditions that Require Consideration

- Bone disease
- Cardiovascular risks
- Liver disease
- Mental health and substance use
- Renal function
- Very high viral load (>750,000 copies/mL)

PREFERRED Initial ART Regimens

Single-Tab Regimens (Rating: A1)	Comments
<p>Abacavir/lamivudine/dolutegravir (ABC/3TC/DTG; Triumeq)</p>	<ul style="list-style-type: none"> • Initiate only in patients confirmed to be negative for HLA-B*5701 • Initiate only in patients with CrCl \geq50 mL/min • Consider underlying risk of coronary heart disease • Documented DTG resistance after initiation in treatment-naïve patients is rare.
<p>Tenofovir alafenamide/emtricitabine/ bictegravir (TAF 25 mg/FTC/BIC; Biktarvy)</p>	<ul style="list-style-type: none"> • Initiate only in patients with CrCl \geq30 mL/min • Contains 25 mg of TAF, unboosted
<p>Tenofovir alafenamide/emtricitabine/ cobicistat/elvitegravir (TAF 10 mg/FTC/COBI/EVG; Genvoya)</p>	<ul style="list-style-type: none"> • Initiate only in patients with CrCl \geq30 mL/min • Carefully consider drug-drug interactions with COBI • Contains 10 mg of TAF, boosted with COBI

PREFERRED Initial ART Regimens

Multi-Tab Regimens with Once-Daily Dosing

Comments

Tenofovir alafenamide/emtricitabine *and* dolutegravir
(TAF 25 mg/FTC *and* DTG;
Descovy *and* Tivicay)

- Rating: A1

- Initiate **only** in patients with CrCl ≥ 30 mL/min
- Documented DTG resistance after initiation in treatment-naïve patients is rare
- Contains 25 mg of TAF, unboosted

Tenofovir alafenamide/emtricitabine *and* raltegravir
(TAF 25 mg/FTC *and* RAL HD; Descovy *and* Isentress HD)

- Rating: A2

- Initiate **only** in patients with CrCl ≥ 30 mL/min
- To date, no clinical trials have been conducted with TAF; data are based on bioequivalence pharmacokinetic studies
- Contains 25 mg of TAF, unboosted
- TAF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets

Notes on Recommended Regimens

- In all cases, FTC and 3TC are interchangeable when not being used in fixed-dose combinations.
- Because of their drug-interaction profiles, COBI and RTV should not be considered interchangeable.
- TAF 10 mg and TAF 25 mg are not interchangeable.
- Refer to the full guideline, Table 9, for dose adjustments based on renal or hepatic function.
- When dosing RAL once daily use the HD formulation of 600 mg tablets dosed at 1200 mg.
- When a “rapid start” or “test and treat” initiation of ART occurs before baseline laboratory test results are available, avoid use of ABC until a patient’s HLA-B*5701 is confirmed negative.
- Clinicians should refer to the DHHS guideline when choosing an initial regimen for women of childbearing potential

Alternative Initial ART Regimens

Single-Tab Regimens	Comments
<p>Tenofovir alafenamide/ emtricitabine/rilpivirine (TAF 25 mg/FTC/RPV; Odefsey)</p> <ul style="list-style-type: none"> • Rating: B3 	<ul style="list-style-type: none"> • Initiate only in patients confirmed to have a CD4 cell count ≥ 200 cells/mm³ and viral load $< 100,000$ copies/mL • Initiate only in patients with CrCl of ≥ 30 mL/min • Use with caution in patients with depression or a history of suicidality • To date, no clinical trials have been conducted; data are based on bioequivalence pharmacokinetic studies • Contraindicated with PPIs • Use H₂-blockers with caution and separate dosing by 12 hrs • Must take with food • Contains 25 mg of TAF, unboosted
<p>Tenofovir disoproxil fumarate/emtricitabine/ cobicistat/elvitegravir (TDF/FTC/COBI/EVG; Stribild)</p> <ul style="list-style-type: none"> • Rating: B1 	<ul style="list-style-type: none"> • Initiate only in patients with CrCl ≥ 70 mL/min • Carefully consider drug-drug interactions with COBI • Consider bone mineral density

Alternative Initial ART Regimens

Multi-Tab Regimens with Once-Daily Dosing	Comments
<p>Tenofovir disoproxil fumarate /emtricitabine <i>and</i> darunavir/ cobicistat (TDF/FTC <i>and</i> DRV/COBI; Truvada <i>and</i> Prezcobix)</p> <ul style="list-style-type: none"> • Rating: B2 	<ul style="list-style-type: none"> • Initiate only in patients with CrCl ≥ 70 mL/min • Carefully consider drug-drug interactions with COBI • Consider bone mineral density
<p>Tenofovir disoproxil fumarate/ emtricitabine <i>and</i> darunavir <i>and</i> ritonavir (TDF/FTC <i>and</i> DRV <i>and</i> RTV; Truvada <i>and</i> Prezista <i>and</i> Norvir)</p> <ul style="list-style-type: none"> • Rating: B1 	<ul style="list-style-type: none"> • Initiate only in patients with CrCl ≥ 50 mL/min • Carefully consider drug-drug interactions with RTV • Consider bone mineral density
<p>Tenofovir disoproxil fumarate /emtricitabine <i>and</i> dolutegravir (TDF/FTC <i>and</i> DTG; Truvada <i>and</i> Tivicay)</p> <ul style="list-style-type: none"> • Rating: B1 	<ul style="list-style-type: none"> • Initiate only in patients with CrCl ≥ 50 mL/min • Documented DTG resistance after initiation in treatment-naïve patients is rare • Consider bone mineral density
<p>Tenofovir disoproxil fumarate/emtricitabine <i>and</i> raltegravir (TDF/FTC <i>and</i> RAL HD; Truvada <i>and</i> Isentress HD)</p> <ul style="list-style-type: none"> • Rating: B1 	<ul style="list-style-type: none"> • Initiate only in patients with CrCl ≥ 50 mL/min • Consider bone mineral density • TDF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets

Alternative Initial ART Regimens

Multi-Tab Regimen with Twice-Daily Dosing	Comments
<p>Tenofovir alafenamide/emtricitabine <i>and</i> raltegravir (TAF 25 mg/FTC <i>and</i> RAL; Descovy <i>and</i> Isentress)</p> <ul style="list-style-type: none"> Rating: B3 	<ul style="list-style-type: none"> Initiate <i>only</i> in patients with CrCl ≥ 50 mL/min TDF/FTC once daily and RAL twice daily

Refer to the full guideline for other ART regimens that are not preferred or alternative regimens.

Contraindicated ART Regimens Based on Routine Lab Parameters

Lab Parameter	Contraindicated ART Regimens	
Viral load $\geq 100,000$ copies/mL	<ul style="list-style-type: none"> • ABC/3TC and COBI/ATV (Epzicom and Evotaz) • ABC/3TC and EFV (Epzicom and Sustiva) • ABC/3TC and RTV and ATV (Epzicom and Norvir and Reyataz) 	<ul style="list-style-type: none"> • RAL and RTV and DRV (Isentress and Norvir and Prezista) • TAF/FTC/RPV (Odefsey) • TDF/FTC/RPV (Complera)
CD4 < 200 cells/mm ³	<ul style="list-style-type: none"> • TAF/FTC/RPV (Odefsey) 	<ul style="list-style-type: none"> • TDF/FTC/RPV (Complera)
CrCl < 70 mL/min	<ul style="list-style-type: none"> • TDF/FTC and COBI/ATV (Truvada and Evotaz) • TDF/FTC/COBI/EVG (Stribild) 	<ul style="list-style-type: none"> • TDF/FTC and COBI/DRV (Truvada and Prezcobix)
CrCl < 50 mL/min	<ul style="list-style-type: none"> • ABC/3TC (Epzicom) • ABC/3TC/DTG (Triumeq) 	<ul style="list-style-type: none"> • TDF/FTC/EFV (Atripla) • TDF/FTC/RPV (Complera)
CrCl < 30 mL/min	<ul style="list-style-type: none"> • TAF/FTC (Descovy) • TAF/FTC/BIC (Biktarvy) • TAF/FTC/COBI/EVG (Genvoya) 	<ul style="list-style-type: none"> • TAF/FTC/RPV (Odefsey) • TDF/FTC (Truvada)

AVOID as Initial ART

ARV	Comments
Nevirapine (NVP; Viramune)	Life-threatening rash: Stevens-Johnson syndrome and toxic epidermal necrolysis are possible
Stavudine (d4T/Zerit); didanosine (ddI/Videx)	Serious toxicities: Potentially fatal lactic acidosis, peripheral neuropathy, pancreatitis, lipodystrophy, and hepatic steatosis are possible
Delavirdine (DLV; Rescriptor)	Thrice-daily dosing and inferior efficacy
Etravirine (ETR; Intelence)	ETR does not have an FDA indication in ART-naïve patients
Maraviroc (MVC; Selzentry)	Inferior efficacy and durability
NRTI-only regimens, either triple or quadruple	Inferior efficacy and durability
Zidovudine (ZDV; Retrovir)	Not well tolerated because of bone marrow suppression (notably anemia), headache, myopathies
Unboosted PIs	Inferior efficacy relative to boosted PIs
Fosamprenavir (FPV/Lexiva); indinavir (IDV/Crixivan); tipranavir (TPV/ Aptivus); nelfinavir (NFV/Viracept)	Either not well studied or limited by dosing and side effects relative to recommended PIs

Key Points

- Neither mental health nor substance use disorders are contraindications to initiating ART, but in some cases, delay may be appropriate.
- COBI and DTG can both cause decreased tubular excretion of creatinine and will dependably cause a slight increase in measured creatinine.
- ABC has been associated with a higher risk of myocardial infarction in some studies, although not in others. No clear causal link has been established.
- Boosted PIs and COBI-boosted EVG are associated with more hyperlipidemia than unboosted INSTIs.
- Consultation with an experienced HIV care provider is advised when a patient's baseline viral load is very high.

Pre-ART Initiation Lab Tests

- Baseline CD4 cell count
- Baseline viral load
- Co-infections: hepatitis B (HBV), hepatitis C (HCV), tuberculosis (TB)
- Creatinine clearance
- Hepatic profile
- HIV genotypic resistance profile
- HLA-B*5701 testing

See full guideline for contraindicated ART regimens based on routine baseline lab parameters and ARV dose adjustments for renal and hepatic impairment

CLINICAL INQUIRY FOR: HIV • HCV • STD • PEP • PrEP

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